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     (FILE 'HOME' ENTERED AT 23:39:28 ON 04 DEC 2003)

     FILE 'USPATFULL' ENTERED AT 23:41:10 ON 04 DEC 2003
L1        393682 S (ALCOHOL (10A) (C1 OR C2 OR C3 OR C4)) OR METHANOL OR ETHANOL
L2         71313 S CARBOMER OR CARBOPOL OR THICKENER OR (THICKENING AGENT) OR (V
L3        168878 S ( SODIUM HYDROXIDE OR NEUTRALIZER)
L4           505 S L1 (1S) L2 (1S) L3
L5           377 S L4 AND (SKIN OR CLEANSING OR CLEANSER OR ANTISEPTIC OR TOPICA
L6           172 S L4 AND (SKIN OR CLEANSING OR CLEANSER OR ANTISEPTIC OR TOPICA
L7             3 S L4/CLM AND (SKIN OR CLEANSING OR CLEANSER OR ANTISEPTIC OR TO
L8        227502 S L1 (30A) (6!% OR 7!% OR 8!% OR 9!%)
L9           130 S L8 AND L6

=> save all
ENTER NAME OR (END):l10068633/l
L# LIST L1-L9 HAS BEEN SAVED AS 'L10068633/L'

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Alclometasone Dipropionate	0.5
Carbomer 940	2.60
Sodium Hydroxide, R	0.04
Propylene Gylcol, USP	200.0
Isopropyl Alcohol, NF	300.0
Hydrochloric Acid	*
Purified Water, USP	q.s. ad to 1.0 g

*Used to adjust the pH to 4.5

13. The method of treating inflammation which comprises applying to the **skin** a **topical** lotion formulation comprising an amount effective to treat said inflammation of a dermatologically acceptable anti-inflamatory corticosteroid in a hydro-alcoholic base consisting essentially of: 15 to 50% by weight of propylene glycol; 20 to 40% by weight of isopropyl alcohol; 20to 60% by weight water; 0.1 to 3.0% by weight of a thickening agent, and sufficient buffer to maintain the pH of the composition within the range of 3.0 to 6.0.

ACCESSION NUMBER: 88:63905 USPATFULL
TITLE: Steroid lotion
INVENTOR(S): Sequeira, Joel A., New York, NY, United States
Munayyer, Farah J., West Caldwell, NJ, United States
Galeos, Rebecca, Bloomfield, NJ, United States
PATENT ASSIGNEE(S): Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)

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PATENT INFORMATION:	US 4775529		19881004	
APPLICATION INFO.:	US 1987-53172		19870521	(7)

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FILE SEGMENT: Granted
PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Maitner, John J., Miller, Stephen I., Nelson, James R.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
LINE COUNT: 291
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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n STN

SUMM [0013] After a series of thorough investigations, the present inventors succeeded in obtaining extracts having potent moisturizing and skin roughness preventive effects by extracting Sphingomonas strain according to a specially designed method, and accomplished the present invention. Thus the first aspect of the invention relates to provide an external composition for skin obtained by washing Sphingomonas strain with acetone, and extracting the resultants with alcohol or alcohol-water mixture. Preferable extracting solutions are **methanol**, **propanol**-water mixture or **butanol**-water mixture. **Propanol** content in **propanol**-water mixture is preferably **75** wt % or below. **Butanol** content in **butanol**-water mixture is preferably **95** wt % or below, and more preferably **85** to **95** wt %, both ends inclusive.

SUMM [0031] As for use of alcohol-water mixture, **propanol**-water mixture and **butanol**-water mixture are preferable. **Propanol** content in **propanol**-water mixture is preferably set not higher than **90%**, and more preferably not higher than **75%**. **Butanol** content in **butanol** -water mixture is preferably set not higher than **95%**, and more preferably between **80** to **95%**.

SUMM [0085] Still other materials compoundable with the external composition for skin of the invention include **thickener** (e.g. carboxyvinyl polymer, carboxymethylcellulose, polyvinyl alcohol, carrageenan, alginate, arginic acid propylene glycol ester, gelatin, electrolyte such as sodium chloride), whitening agent (e.g. arbutin, allantoin, vitamin E derivative, glycyrrhizin, ascorbic acid phosphoric acid magnesium salt, Kojic acid, panteric acid derivative, placenta extract, coix seed, green tea, pueraria root, mulberry bark, licorice, scutellaria root, aloe, bitter orange peel, German chamomile, Ganoderma lucidum), skin protector (e.g. retinol, retinol ester, retinoic acid), skin emollient agent (e.g. stearyl alcohol, glyceryl monoricinoleate, mink oil, cetyl alcohol, stearic acid, palm oil, castor oil, oxostearic acid), skin relaxing agent (e.g. stearyl alcohol, glycerin monoricinoleate, glycerin monostearate, cetyl alcohol), skin permeation accelerator (e.g. 2-methylpropane-2-ol, 2-**propanol**, ethyl-2-hydroxypropanoate, 2,5-hexiandiol, acetone, tetrahydrofuran), biologically active plant extract (e.g. extracts from aloe, arnica, licorice, sage or swertia herb), preservative (e.g. p-hydroxybezoate, sodium benzoate, urea, metylparaben, ethylparaben, propylparaben, butylparaben), anti-inflammatory (e.g. .alpha.-tocopherol, butylhydroxytoluene), buffer (e.g. combination of lactic acid with triethanolamine or **sodium hydroxide**), keratin solubilizer (e.g. lactic acid, glycollic acid, malic acid, tartaric acid, citric acid), scrubbing material (e.g. polyethylene powder), and pigment (e.g. lake of calcium, barium or aluminum, iron oxide, titanium dioxide, mica).

DETD [0102] After sterilizing the resulted culture liquor and adjusting its pH at 5.0, the fungus body was collected by centrifugation. Twenty kg of the fungus body was then added with 30 liters of acetone, stirred, and collected by filtration. Thus obtained fungus body was extracted three times with 30 liters each of solvent shown in Table 4, and resultant extracts were distilled using a flash evaporator to remove the solvent. Four liters of residual liquor is added with 8 liters of acetone, stirred, and allowed to stand for precipitation. The precipitate was collected, added with another 2 liters of acetone, and again allowed to stand to produce the precipitate. The precipitate was finally collected, dewatered, and dried under reduced pressure to prepare the composition comprising sphingoglycolipid (Samples 1 to 19).

TABLE 4

Sample No.	Solvents	Mixing ratio
1	**Methanol**	
2	**Methanol**/water	**85**/15
3	**Methanol**/water	**70**/30
4	**Methanol**/water	55/45
5	**Ethanol**	
6	**Ethanol**/water	**85**/15
7	**Ethanol**/water	**70**/30
8	**Ethanol**/water	55/45
9	**Propanol**	
10	**Propanol**/water	**85**/15
11	**Propanol**/water	**70**/30
12	**Propanol**/water	55/45
13	**Isopropanol**	
14	**Isopropanol**/water	**85**/15
15	**Isopropanol**/water	**70**/30
16	**Isopropanol**/water	55/45
17	**Butanol**	
18	**Butanol**/water	**85**/15
19	**Methanol**/chloroform	**75**/25

DETD [0106] Individual components listed below were mixed at room temperature and thoroughly stirred to produce a toilet lotion.

TABLE 8

Components	weight part
Active component	1.0
Methylparaben	0.1
Polyoxyethylene hydrogenated castor oil	1.2
Polyoxyethylene sorbitol oleate	0.4
Ethanol	5.3
Purified water	**92**.0

DETD [0110] Individual components listed below were mixed at room temperature and thoroughly stirred to produce a pre-shaving lotion.

TABLE 12

Components	weight part
Active component	1.0
Zinc sulfophenolate	1.0
Isopropylmyristic acid ester	7.0
Isopropylpalmitic acid ester	8.0
Ethanol	**82**.5
Perfume	0.5

DETD [0123] Individual components listed below were mixed at room temperature to produce a hair dye.

TABLE 25

Components	weight part
Active component	3.0
Pigment	1.0
Acrylic resin alkanolamine (50%)	8.0
Perfume	0.5
Ethyl alcohol	**88**.0

CLM What is claimed is:

1. An external composition for **skin** comprising a component extracted from a fungus of genus Sphingomonas.

2. An external composition for **skin** according to claim 1, wherein said component is obtained by washing said fungus of genus Sphingomonas with acetone, and then extracting the resultant with alcohol or alcohol-water mixture.

3. An external composition for **skin** according to claim 2, wherein said alcohol or alcohol-water mixture is methanol, propanol-water mixture or butanol-water mixture.

4. An external composition for **skin** according to claim 3, wherein said alcohol or alcohol-water mixture is **propanol** -water mixture having a **propanol** content of **75** wt % or less, or **butanol**-water mixture having a **butanol** content of **95** wt % or less.

5. An external composition for **skin** according to claim 4, wherein said alcohol or alcohol-water mixture is **butanol**-water mixture having a **butanol** content ranging from **80** to **95** wt %.

6. An external composition for **skin** according to claim 1, wherein said fungus of genus Sphingomonas is a white fungus.

7. An external composition for **skin** comprising a sphingoglycolipid represented by the following formula: ##STR5## where, R.sub.1 represents a sugar portion consisting of a single uronic acid or one to four hexoses selected from a group consisting of uronic acid, glucosamine, galactose and mannose; R.sub.2 represents an alkyl group which may have a cycloalkyl group, an alkenyl group or an alkynyl group; and R.sub.3 represents an alkyl group; these alkyl, alkenyl and alkynyl groups being straight or branched, and substituted or unsubstituted.

8. An external composition for **skin** according to claim 7, wherein said R.sub.1 consists of 3 or 4 hexoses.

9. An external composition for **skin** according to claim 8, wherein said R.sub.1 is a sugar portion of four hexoses consisting of a uronic acid, a glucosamine, a galactose and a mannose; three hexoses cosisting of a uronic acid, a glucosamine and a galactose; or four hexoses consisting of a uronic acid, a galactose and two glucoses.

10. An external composition for **skin** according to claims 7, wherein said R.sub.2 is represented by any one of the following formulae: ##STR6##

11. An external composition for **skin** according to claim 7, wherein said R.sub.2 has 15 to 25 carbon atoms.

12. An external composition for **skin** according to claim 11, wherein said R.sub.2 is represented by any one of the following formulae: ##STR7##

13. An external composition for **skin** according to claim 7, wherein said R.sub.3 is a substituted or unsubstituted straight alkyl group having 10 to 20 carbon atoms.

14. An external composition for **skin** according to claim 13, wherein said R.sub.3 is a straight alkyl group having 12 carbon atoms.

15. An external composition for **skin** according to claim 7, wherein said R.sub.1 has a structure represented by any one of formulae A to D as in claim 10, R.sub.2 has a structure represented by any one of formulae a to c as in claim 12.

16. Use of said external composition for **skin** as claimed in claim 1 for toilet soap, shampoo, **cleansing** foam, rinse, eye cream, eye shadow, cream or milky lotion, toilet lotion, perfume, face powder, facial oil, hair-care cosmetics, hair dye, jelly fragrance, powder, pack, shaving cream, shaving lotion, suntan oil, anti-suntan oil, suntan lotion, sun-screening lotion, suntan cream, sun-screening cream, foundation, powdery fragrance, cheek rouge, mascara, eyebrow pencil, nail cream, nail enamel, nail enamel remover, hair cleaner, bath cosmetics, lipstick, lip cream, eyeliner, toothpaste, deodorant agent, eau de cologne, hair tonic, hair restorer, ointment, wet pack, medicated lip cream or anti-atopic agent.

17. An external composition for **skin** according to claim 1 further comprising at least one of whitening agent, surfactant, dye, perfumery, aseptic agent, pigment, mildewproof agent, antioxidant, UV absorber, infrared absorber, fluorescent material, metal ion blocker, binder, filler, antiphlogistic, circulation accelerator, cell activator and antibiotic.

PI	US 2002006414	A1	20020117
	US 6348201	B2	20020219

sorbitol esters, 1,2,6-hexanetriol, **ethanol**, **isopropanol**, butanediol, and mixtures thereof. These solutions contain from about 1% to about 20%, preferably from about 2% to about 10%, of the chelating agent, and from about **80%** to about **99%**, preferably from about 90% to about 98%, of an acceptable organic solvent.

SUMM Various water-soluble materials may also be present in the compositions of this invention. These include humectants, such as glycerol, sorbitol, propylene glycol, alkoxylated glucose and hexanetriol, **ethyl** cellulose, polyvinyl **alcohol**, carboxymethyl cellulose, vegetable gums and clays such as Veegum.RTM. (magnesium aluminum silicate, R. T. Vanderbilt, Inc.); proteins and polypeptides; preservatives such as the methyl, ethyl, propyl and butyl esters of hydroxybenzoic acid (Parabens--Mallinckrodt Chemical Corporation), EDTA, methylisothiazolinone and imidazolidinyl ureas (Germall 115--Sutton Laboratories); and an alkaline agent such as **sodium hydroxide** or potassium hydroxide to neutralize, if desired, part of the fatty acids or **thickener** which may be present. In addition, the topical compositions herein can contain conventional cosmetic adjuvants, such as dyes, opacifiers (e.g., titanium dioxide), pigments and perfumes.

CLM What is claimed is:

1. A method of inhibiting the deleterious effects of chronic ultraviolet light exposure to **skin**, such deleterious effects including one or more of **skin** cancer or premature aging as characterized by **skin** wrinkling, **skin** yellowing, **skin** cracking, telangiectasis, solar keratoses, ecchymoses, or lack of elasticity, comprising applying to the **skin**, prior to exposing the **skin** to ultraviolet light, a safe and photoprotectively effective amount of a nonsunscreen chelating agent selected from the group consisting of 2,2'-dipyridylamine; 1,10-phenanthroline; di-2-pyridylketone; 2-furildioxime; 2,3-bis(2-pyridyl)pyrazine; 1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)-pyridone; 2,3-dihydroxybenzoic acid; ethylenediamine-N,N-bis(2-hydroxyphenylacetic acid), dimethyl ester; 1,1'-carbonyldiimidazole; 1,2-dimethyl-3-hydroxypyrid-4-one; 2,4,6-tri(2-pyridyl)-1,3,5-triazine; 1-pyrrolidinecarbodithioic acid; diethyldithiocarbamic acid; 6-cyclohexyl-1-hydroxy-4-methyl-2(1H)-pyridinone; 2,2'-dipyridyl; 1,2-cyclohexanedione dioxime; 3-hydroxy-2-methyl-4-pyrone; 2,3-bis(2-pyridyl)-5,6-dihydropyrazine; 3-(4-phenyl-2-pyridyl)-5-phenyl-1,2,4-triazine; 5-hydroxy-2-(hydroxymethyl)-4H-pyran-4-one; 2,3-dihydroxypyridine; 2,2'-biquinoline; 2,2'-bipyrazine; 3-(2-pyridyl)-5,6-diphenyl-1,2,4-triazine; 4,4'-dimethyl-2,2'-dipyridyl; 4,5-dihydroxy-1,3-benzene-disulfonic acid; phenyl 2-pyridyl ketoxime; desferrioxamine B; 5,7-dichloro-8-hydroxyquinoline; 2,3-dihydroxynaphthalene; 2,3,5,6-tetrakis-(2'-pyridyl)pyrazine; 2,4-bis(5,6-diphenyl-1,2,4-triazine-3-yl)pyridine; di-2-pyridyl glyoxal; 6-hydroxy-2-phenyl-3(2H)-pyridazinone; 2,4-pteridinediol; 3-(4-phenyl-2-pyridyl)-5,6-diphenyl-1,2,4-triazine; N-benzoyI-N-phenylhydroxylamine; 3-amino-5,6-dimethyl-1,2,4-triazine; 2,6-pyridinedicarboxylic acid; 2,4,5-trihydroxypyrimidine; and 4-(2-amino-1-hydroxyethyl)-1,2-benzenediol.

13. The method of claim 1 wherein from about 0.001 mg/cm.sup.2 to about 1 mg/cm.sup.2 of the chelating agent is applied to the **skin**.

14. The method of claim 10 wherein from about 0.01 mg/cm.sup.2 to about 0.5 mg/cm.sup.2 of the chelating agent is applied to **skin**.

15. The method of claim 1 wherein a safe and photoprotectively effective amount of a sunscreening agent is simultaneously applied to the **skin**.

16. The method of claim 1 wherein a safe and photoprotectively effective amount of an anti-inflammatory agent is simultaneously applied to the **skin**.

17. The method of claim 14 wherein from about 0.01 mg/cm.sup.2 to about 0.5 mg/cm.sup.2 of a sunscreening agent selected from the group consisting of 2-ethylhexyl p-methoxycinnamate, butylmethoxydibenzoylmethane, 2-hydroxy- 4-methoxybenzophenone, octyldimethyl p-aminobenzoic acid, the 4-N,N-(2-ethylhexyl)methylaminobenzoic acid ester of 2,4-dihydroxybenzophenone, the N,N-di-(2-ethylhexyl)-4-aminobenzoic acid ester of 4-hydroxydibenzoylmethane, the 4-N,N-(2-ethylhexyl)methylaminobenzoic acid ester of 4-hydroxydibenzoylmethane, the 4-N,N-(2-ethylhexyl)methylaminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy) benzophenone, the 4-N,N-(2-ethylhexyl)methylaminobenzoic acid ester of 4-(2-hydroxyethoxy)dibenzoylmethane, the N-N-di-(2-ethylhexyl)-4-aminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy)benzophenone, the N,N-di-(2-ethylhexyl)-4-aminobenzoic acid ester of 4-(2-hydroxyethoxy)dibenzoylmethane and mixtures thereof, is simultaneously applied to the **skin**.

18. A **topical** photoprotective composition comprising: (a) a safe and photoprotectively effective amount of a non-sunscreen chelating agent selected from the group consisting of 2,2'-dipyridylamine; 1,10-phenanthroline; di-2-pyridylketone; 2-furildioxime; 2,3-bis(2-pyridyl)pyrazine; 2,3-dihydroxybenzoic acid; ethylenediamine-N,N-bis(2-hydroxyphenylacetic acid), dimethyl ester; 1,1'-carbonyldiimidazole; 2,4,6-tri(2-pyridyl)-1,3,5-triazine; 2,2'-dipyridyi; 1,2-cyclohexanedione dioxime; 3-hydroxy-2-methyl-4-pyrone; 2,3-bis(2-pyridyl)-5,6-dihydropyrazine; 3-(4-phenyl-2-pyridyl)-5-phenyl-1,2,4-triazine; 2,3-dihydroxypyridine; 2,2'-biquinoline; 2,2'-bipyrazine; 3-(2-pyridyl)-5,6-diphenyl-1,2,4-triazine; 4,4'-dimethyl-2,2'-dipyridyl; 4,5-dihydroxy-1,3-benzene-disulfonic acid; phenyl 2-pyridyl ketoxime; desferrioxamine B; 5,7-dichloro-8-hydroxyquinoline; 2,3-dihydroxynaphthalene; 2,3,5,6-tetrakis-(2'-pyridyl)pyrazine; 2,4-bis(5,6-diphenyl-1,2,4-triazine-3-yl)pyridine; di-2-pyridyl glyoxal; 6-hydroxy-2-phenyl-3(2H)-pyridazinone; 2,4-pteridinediol; 3-(4-phenyl-2-pyridyl)-5,6-diphenyl-1,2,4-triazine; N-benzoyl-N-phenyl-hydroxylamine; 3-amino-5,6-dimethyl-1,2,4-triazine; 2,4,5-trihydroxypyrimidine; and 4-(2-amino-1-hydroxyethyl)-1,2-benzenediol; and (b) a safe and effective amount of a **topical** carrier comprising a safe and effective amount of an emollient.

PI US 5487884 19960130

Compound I, finely milled	1.0	g
2. **Carbopol** 934	0.6	g
3. **Sodium hydroxide**	q.s. ad pH 6	
4. **Ethanol, 94%**	50.0	g
5. Demineralized water	ad 100.0	g

DETD The active ingredient is incorporated into the **94% ethanol**/water mixture with protection from light. **Carbopol** 934 is stirred in until gelling is complete and the pH value is adjusted with **sodium hydroxide**.

CLM What is claimed is:

1. A method of treating photodamaged **skin** comprising topically administering to said photodamaged **skin** a composition which comprises a compound of the formula: ##STR23## wherein R.sup.2 is C.sub.2-8 -alkanoyl, C.sub.2-8 -alkyl, C.sub.2-8 -alkenyl, C.sub.2-8 -alkynyl or --OCH.sub.2 R.sup.3 ; R.sup.3 is hydrogen, C.sub.1-6 -alkyl, C.sub.2-6 -alkenyl or C.sub.2-6 -alkynyl; R.sup.5 and R.sup.7 each independently are hydrogen or C.sub.1-5 -alkyl; R.sup.4 and R.sup.6 each independently are hydrogen or C.sub.1-5 -alkyl, or taken together are methylene or ethylene which are unsubstituted or substituted by hydroxy; R.sup.a, R.sup.a', R.sup.b and R.sup.b' each are independently hydrogen or C.sub.1-5 -alkyl; R.sup.10 is carboxyl, C.sub.1-6 -alkoxycarbonyl or mono- or di-(C.sub.1-6 -alkyl)carbamoyl; and pharmaceutically acceptable salts of carboxylic acids of formula Ie; and a pharmaceutically acceptable carrier, wherein said composition is administered in an amount sufficient to treat said photodamaged **skin**.

PI US 5700836 19971223

DETD The commercially available products were: Gelufene.RTM. (ibuprofen 5%, **isopropyl alcohol**, hydroxyethylcellulose, **sodium hydroxide**, benzyl alcohol and purified water), Dolgit.RTM. cream (ibuprofen 5%, medium chain triglycerides, mixture of glycerol monostearate and polyoxyethylene stearates, polyoxyethylene fatty acid esters, xanthan gum, lavender oil, neroli oil, water, propylene glycol, parahydroxybenzoate of methyl soda), Ibutop.RTM. (ibuprofen 5%) (Laboratoire Chefaro-Ardeval, Saint-Denis Cedex, France) and Deep Relief.TM. gel (ibuprofen 5%, menthol, **Carbomer**, propylene glycol, di-isopropanolamine, **ethanol**, purified water).

DETD This is example is designed to demonstrate the effect of concentration of ibuprofen (IB) on flux and total delivery (24 h) for formulations with and without propylene glycol. The test were run under the same conditions as in Example 1 except that human skin was used, an **80**/20 mixture of PBS and **ethanol** was used as the receptor fluid, and the pH was adjusted to 7.7 with sodium hydroxide; the test compositions which were prepared and tested (the enhancer was 2-n-nonyl-1,3-dioxolane) are shown in the following Table 6:

DETD This example illustrates the effect of propylene glycol (PG) on delivery of various NSAIDs from aqueous formulations containing 10 wt. % of skin penetration enhancer, 2-n-nonyl-1,3-dioxolane. All the tested formulations included **ethanol** and water at a **70**:30 weight ratio and were neutralized with base to a pH of about 7. The tests were run in standard static cells under substantially the same conditions as described in Example 1 but using human skin rather than procine skin. The tested compositions and results are shown in the following Table 10.

DETD This example further illustrates the effects of PG on drug delivery (0.5% piroxicam) at two different levels of the enhancer, 2-n-nonyl-1,3-dioxolane (5% or 10%) versus a control (0% enhancer, 0% PG) and a commercial product, Geldene.RTM. (0.5% piroxicam in the form of its diisopropanolamine (DIPA) salt; approximately 24% **ethanol** ; >0 PG). In the compositions according to the invention and the control triethanolamine (TEA) was used as the base to neutralize the piroxicam and the vehicle was **ethanol**:water (**70**:30). The formulations and test procedures were, otherwise, as described in Example 8. The results are shown below in Table 11.

DETD This example further illustrates the effects of the invention with diclofenac as the NSAID. The test procedure was substantially the same as previously described using either human (H) or porcine (P) skin and an **ethanol**:water (**70**:30) vehicle. 2-n-nonyl-1,3-dioxolane was used as the skin permeation enhancer compound according to the invention. The results are shown in Table 12 below. In Run Nos. 10-A through 10-G 1 wt. % of diclofenac (as free acid) was used. In Run Nos. 10-I and 10-J (commercial product) 0.93 wt. % of diclofenac (as free acid) was used.

CLM What is claimed is:

1. A substantially neutral ibuprofen containing alcoholic or aqueous alcoholic composition which comprises, on a weight basis, of the total composition: a therapeutically effective amount, in the range of from about 2 to 10% ibuprofen in the form of its pharmacologically acceptable salt; a **skin** penetration enhancing effective amount in the range of from about 4 to 15% of a C.sub.7 to C.sub.14 -hydrocarbyl substituted 1,3-dioxolane, 1,3-dioxane or acetal; 0 to about 18% of glycol having from 3 to 6 carbon atoms; at least about 40% of volatile alcohol selected from the group consisting of ethanol, isopropanol and mixture thereof; 0 to about 25% water; base to provide a pH in the range of from 6.5 to about 8, and, optionally, gelling agent effective to thicken the composition to avoid or minimize run-off when applied to the **skin**.

2. The composition according to claim 1 which comprises from about 2 to about 10% said salt of ibuprofen; from about 4 to about 15% of the

enhancer wherein the alkyl group substituent has from about 7 to about 10 carbon atoms; from about 0 to about 15% propylene glycol; from about 55 to about **70% ethanol**; from about 4 to about 25% water; base in amount to adjust the pH of the composition in the range of from 6.5 to about 7.5, and, 0 to about 2% of gelling agent.

3. A glycol-free **topical** composition effective for the transdermal administration of naproxen, which comprise, on a weight basis of the total composition: a pharmaceutically effective amount of naproxen, from about 2 to about 20% of 2-C.sub.7 -C.sub.14 hydrocarbyl substituted 1,3-dioxolane, 1,3-dioxane, or acetal **skin** penetration enhancer; from about 35 to about **85% ethanol**, iso-**propanol**, or mixture thereof; 0 to about 40% water; base in an amount to provide a pH in the range of from about 6 to about 8, and up to about 5% gelling agent.

4. A method for the transdermal administration of ibuprofen to a patient in need thereof which comprises topically applying to the **skin** of the patient a substantially neutral composition comprising from about 5 to about 15 weight percent of ibuprofen in the form of its pharmacologically acceptable salt in a vehicle comprising a lower alcohol selected from the group consisting of **ethanol**, **isopropanol** and mixture thereof, alkyl glycol having from 3 to 6 carbon atoms, and water in a mixing ratio of alcohol:glycol:water of 40-**80**:0-20:0-25, said vehicle comprising from about 70 to about 90 weight percent of the composition, and from about 5 to about 15 weight percent of a **skin** penetration enhancing compound selected from the group consisting of 2-hydrocarbyl-1,3-dioxolane, 2-hydrocarbyl-1,3-dioxane and hydrocarbyl substituted-acetal, wherein the hydrocarbyl group has from 7 to 14 carbon atoms, and base in amount to provide a pH in the range of from 6.5 to about 8.

5. A method for the transdermal administration of naproxen to a patient in need thereof which comprises topically applying to the **skin** of the patient a substantially neutral composition comprising a therapeutically effective amount of naproxen in a glycol-free vehicle comprising a lower alcohol selected from the group consisting of **ethanol**, **isopropanol** and mixture thereof, and water in a mixing ratio of alcohol:water of 35-**85**:10-40, said vehicle comprising from about **70** to **90** weight percent of the composition, and from about 2 to 20 weight percent of a **skin** penetration enhancing compound selected from the group consisting of 2-hydrocarbyl-1,3-dioxolane, 2-hydrocarbyl-1,3-dioxane and hydrocarbyl substituted-acetal, wherein the hydrocarbyl has from 7 to 14 carbon atoms, and base in amount to provide a pH in the range of from 6.5 to about 8.

6. The composition according to claim 2 which comprises from about 2 to about 10% said salt of ibuprofen; from about 5 to about 10% of the enhancer; about 0% propylene glycol; from about 55 to about **70 % ethanol**; from about 4 to about 25% water; base in amount to adjust the pH of the composition to from 6.5 to about 7.5; and 0 to 2% gelling agent.

7. The composition according to claim 2 which comprises from about 2 to about 10% said salt of ibuprofen; from about 5 to about 10% of the enhancer; from about 1 to about 15% propylene glycol; from about 55 to about **70% ethanol**; from about 4 to about 25% water; base in amount to adjust the pH of the composition to from 6.5 to about 7.5; and 0 to about 2.0% gelling agent.

9. The composition of claim 2 which comprises about 5% of said salt of ibuprofen; from about 5 to about 10% **skin** penetration enhancer wherein the hydrocarbyl group substituent is an alkyl group having from

about 7 to about 10 carbon atoms; up to about 5% propylene glycol; from about 55 to about **70% ethanol**; water in amount to provide an **ethanol**:water ratio, by weight, of about **70** :30; base in amount to adjust the pH of the composition in the range of from 6.5 to about 7.5, and, gelling agent in amount effective to thicken the composition.

11. A substantially neutral alcoholic or aqueous alcoholic **topical** composition effective for the transdermal delivery of non-steroidal anti-inflammatory drug which comprises 0.1 to 10% diethylamine salt of diclofenac; from about 2 to about 15% of C.sub.7 to C.sub.14 -hydrocarbyl derivative of 1,3-dioxolane, 1,3-dioxane or acetal as **skin** penetration enhancer; up to about 30% propylene glycol; from about 45 to about **70%** of volatile alcohol selected from the group consisting of **ethanol**, **isopropanol** and mixtures thereof; up to about 20% water; base to provide a pH in the range of from about 6.5 to about 75; and up to about 5% gelling agent.

12. The composition of claim 1 which comprises 2-n-nonyl-1,3-dioxolane as **skin** penetration enhancing compound.

13. The composition of claim 3 which comprises 2-n-nonyl-1,3-dioxolane as **skin** penetration enhancing compound.

PI US 5976566 19991102

DETD Prepare a 4% solution of **sodium hydroxide** in water. Heat the purified water to **60**.degree. C. Add **carbomer** 940 and mix at high speed until dispersed. Cool the above mixture to room temperature and slowly charge **sodium hydroxide** until uniform. Add **80%** of **isopropyl alcohol** to the above with mixing. Dissolve the active compound in remaining **isopropanol**. Add this to the mixture with stirring. Adjust pH to 5.0 to 5.5 with **sodium hydroxide**, if necessary.

CLM What is claimed is:

1. A method of treating hyperproliferative **skin** disease in a mammal comprising administering to said mammal an anti-hyperproliferative **skin** disease effective amount of a compound of formula I ##STR5## wherein: W and X may be the same or different and represent CH or N; Y and Z may be the same or different and are O or S; R.sup.5 and R.sup.6 may be the same or different and are hydrogen, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms trifluoromethyl, alkylthio having 1 to 6 carbon atoms or cyano; R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently hydrogen, alkyl having 1 to 6 carbon atoms, CH.sub.2 OH, CO.sub.2 R.sup.7 {wherein R.sup.7 is hydrogen or alkyl having 1 to 6 carbon atoms} or hydroxy, provided that only one group on any carbon atom is --OH and that such carbon atom is not adjacent to a heteroatom; V is oxygen, S(O).sub.n {wherein n is 0, 1 or 2}, or N--R.sup.8 {wherein R.sup.8 is hydrogen, alkyl having from 1 to 6 carbon atoms, carboxylic acyl having from 2 to 7 carbon atoms, sulfonylalkyl having from 1 to 6 carbon atoms, carboalkoxy having from 2 to 7 carbon atoms, CONH.sub.2, phenyl, pyridinyl of which the last two may be substituted with up to three of any of the following substituents, Q: hvdroxy, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms, trifluoromethyl, cyano, cycloalkyl having from 3 to 7 carbon atoms, alkenyloxy having from 3 to 6 carbon atoms, alkynyloxy having from 3 to 6 carbon atoms, S(O).sub.n --R.sup.a (wherein n is defined herein and R.sup.a is alkyl having from 1 to 6 carbon atoms), NHSO.sub.2 R.sup.a (wherein R.sup.a is defined herein), NHSO.sub.2 CF.sub.3, NHCOCF.sub.3, SO.sub.2 NH.sub.2, COR.sup.b (wherein R.sup.b is OH, NH.sub.2, NHR.sup.a or OR.sup.a wherein R.sup.a is defined herein), O--B--COR.sup.1 (wherein B is alkanediyl having from 1 to 4 carbon atoms and R.sup.b is defined herein), or NHCOR.sup.c (wherein R.sup.c is hydrogen, alkyl having from 1 to 6 carbon atoms, alkoxy having from 1 to 6 carbon atoms, COR.sup.d (wherein R.sup.d is hydroxy or alkoxy having from 1 to 6 carbon atoms) or NHR.sup.e (wherein R.sup.e is hydrogen or alkyl having 1 to 6 carbon atoms))}; r is 0, 1 or 2; a is an integer of from 2 to 6; and A is phenyl, naphthylenvl, indenyl, indanyl, pyridinyl, pyrimidinyl, pyrazinyl, furanyl, thienyl, imidazolyl, thiazolyl or oxazolyl any of which may be substituted with up to three substituents, Q as defined herein.

PI US 4775524 19881004

Ingredients:

1.	Compound Ia, finely milled	3.0	g
2.	**Carbopol** 934	0.6	g
3.	**Sodium hydroxide** q.s.	ad pH 6	
4.	**Ethanol**, **94%**	50.0	g
5.	Demineralized water ad	100.0	g

DETD The active substance is incorporated into the **ethanol**, (**94%**)/water mixture under protection from light. **Carbopol** 934 is stirred in until gelling is complete and the pH value is adjusted with **sodium hydroxide**.

CLM What is claimed is:

14. The method of claim 13 wherein said treated primary malignancy is an epithelial carcinoma of the breast, **skin**, colon, bladder, esophagus, stomach, larynx, lung or oral cavity.

23. The method of claim 22 wherein said tumors are selected from the group consisting of epithelial tumors of the breast, **skin**, colon, bladder, esophagus, stomach, larynx, lung or oral cavity.

PI US 4863969 19890905

7. A high alcohol content gel composition with **skin** moisturizing and conditioning properties comprising (a) from about **60** to **65** weight percent of **ethanol**; (b) from about 0.45 to 0.65 weight percent of a thickening agent which is an addition polymer of acrylic acid crosslinked with an unsaturated polyfunctional agent; (c) a sufficient amount of a compatible neutralizing agent for thickening agent (b) to neutralize from about 15% to 50% of acrylic acid carboxyl units present in thickening agent (b), said neutralizing agent being selected from the group consisting of amines of the formula HO(C.sub.m H.sub.2m).sub.2 NH where m has a value of from 2 to 3, aminomethyl propanol, aminomethyl propanediol, and H(OCH.sub.2 CH.sub.2).sub.x RN(CH.sub.2 CH.sub.2 O).sub.y H where R is a hydrocarbon radical having from 10 to 18 carbon atoms and the sum of x+y has an average value of from about 5 to 25; (d) from about 0.75 to 2 weight percent of at least one hydrocarbon emollient selected from the group consisting of petrolatum and mineral oil; (e) from about 0.5 to 1.5 weight percent of at least one fatty ester emollient; (f) from about 0.1 to 0.5 weight percent of at least one compatible surfactant to stabilize the composition; (g) from about 1 to 2.5 weight percent of at least one fatty alcohol having from 12 to 22 carbons atoms; (h) from about 2 to 4 weight percent of a humectant selected from the group consisting of water soluble polyhydric alcohols having from 2 to 3 hydroxyl groups; (i) up to about 0.5 weight percent of a compatible hydroxypropyl guar gum thickening agent; and (j) the balance comprising water, there being at least about 20 weight percent water present and the gel composition has a viscosity of from about 10,000 centipoise to 50,000 centipoise at 25.degree. C.

PI US 4956170 19900911

DETD Prepare a 4% solution of **sodium hydroxide** in water. Heat the purified water to **60**.degree. C. Add **carbomer** 940 and mix at high speed until dispersed. Cool the above mixture to room temperature and slowly charge **sodium hydroxide** solution until uniform. Add **80%** of **isopropyl alcohol** to the above with mixing. Dissolve the active compound in remaining **isopropyl alcohol**. Add this to the mixture with stirring. Adjust pH to 5.0 to 5.5 with **sodium hydroxide**, if necessary.

CLM What is claimed is:

6. A method for treating hyperproliferative **skin** diseases in a mammal which comprises topically administering an effective amount of a pharmaceutical composition defined in claim 2 to said mammal.

PI US 5011860 19910430